We claim:

1. Use of a histone deacetylase inhibitor, or a pharmaceutically acceptable salt thereof or a pharmaceutically acceptable prodrug thereof, for the preparation of a medicament, for the treatment, prevention or suppression of an immune disorder, immune response or immune mediated response.

2. Use of a histone deacetylase inhibitor, or a pharmaceutically acceptable salt thereof or a pharmaceutically acceptable prodrug thereof, for the preparation of a medicament, for the prevention or treatment of acute or chronic transplant rejection in a recipient patient of an organ, tissue or cell transplant.

3. Use histone deacetylase inhibitor, or a pharmaceutically acceptable salt thereof or a pharmaceutically acceptable prodrug thereof, for the preparation of a medicament, for use in enhancing graft survival following transplant, by administering to an animal previous to, concurrently with, or subsequent to a transplant procedure an effective amount of the histone deacetylase inhibitor compound.

4. Use of a histone deacetylase inhibitor, or a pharmaceutically acceptable salt thereof or a pharmaceutically acceptable prodrug thereof, for the preparation of a medicament, for use in combination with a second pharmacologically active agent or a pharmaceutically acceptable salt thereof or a pharmaceutically acceptable prodrug thereof, for the treatment, prevention or suppression of an immune disorder, immune response or immune mediated response.

5. Use of a histone deacetylase inhibitor, or a pharmaceutically acceptable salt thereof or a pharmaceutically acceptable prodrug thereof, for the preparation of a medicament, for use in combination with a second pharmacologically active agent or a pharmaceutically acceptable salt thereof or a pharmaceutically acceptable prodrug thereof, for the prevention or treatment of acute or chronic transplant rejection in a recipient patient of an organ, tissue or cell transplant.

6. Use histone deacetylase inhibitor, or a pharmaceutically acceptable salt thereof or a pharmaceutically acceptable prodrug thereof, for the preparation of a medicament, for use in combination with a second pharmacologically active agent or a pharmaceutically acceptable salt thereof or a pharmaceutically acceptable prodrug thereof, for use in enhancing graft survival

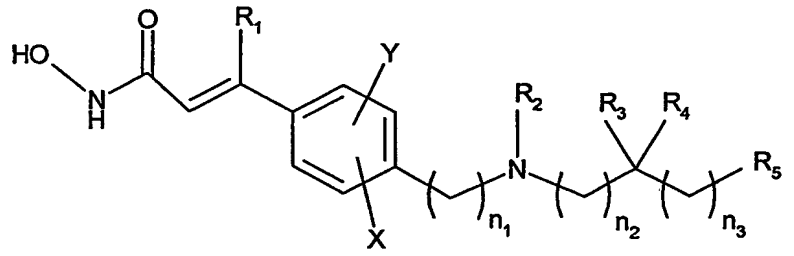
following transplant, by administering to an animal previous to, concurrently with, or subsequent to a transplant procedure an effective amount of the histone deacetylase inhibitor compound.

7. The use according to any one of claims 4-6 wherein the second pharmacologically active agent is selected from immunosuppressive agents, immunomodulating agents, steroids, NSAIDS or mixtures thereof.

8. The use according to claim 7 wherein the second pharmacologically active agent is selected from sphingosine 1-phosphate receptor agonist, e.g. FTY-720 or an analog thereof, mTOR inhibitors, e.g. rapamycin, 40-O-(2-hydroxyethyl)-rapamycin; calcineurin inhibitors, cyclosporine, CCI779, ABT578, a rapalog or AP23573, AP23464, AP23675 or AP23841; TAFA93, biolimus-7, biolimus-9, an ascomycin having immunosuppressive properties, e.g. ABT-281, ASM981, etc.; cyclophosphamide; methotrexate; a somatostatin analogue like octreotide, lanreotide, vapreotide or SOM230; a deoxyspergualine compound or derivative or analog thereof, e.g. 15-DSG, monoclonal antibodies to leukocyte receptors, e.g., MHC, CD2, CD3, CD4, CD7, CD8, CD11a/CD18, CD25, CD27, CD28, CD40. CD45, CD58, CD80, CD86, CD134, CD137, ICOS, CD150 (SLAM), CD152, OX40, 4-1BB or to their ligands, e.g. CD154, or antagonists thereof; other immunomodulatory compounds, e.g. a recombinant binding molecule having at least a portion of the extracellular domain of CTLA4 or a mutant thereof, e.g. an at least extracellular portion of CTLA4 or a mutant thereof joined to a non-CTLA4 protein sequence, e.g. CTLA4Ig (for ex. designated ATCC 68629) or a homologue or a mutant thereof, e.g. LEA29Y; adhesion molecule inhibitors, e.g. LFA-1 antagonists, ICAM-1 or -3 antagonists, anti-LFA-1 or anti-ICAM antibodies, VCAM-4 antagonists or VLA-4 antagonists; or anti-chemokine antibodies or anti-chemokine receptor antibodies or low molecular weight chemokine receptor antagonists, e.g. anti MCP-1 antibodies, and mixtures thereof.

9. A use according to any one of claims 1-8 wherein the histone deacetylase inhibitor has an IC50 of <500 nM in the mouse or human mixed lymphocyte reaction (MLR).

10. A use according to any one of claims 1-9 wherein the histone deacetylate inhibitor is



(I)

wherein

R_1 is H, halo, or a straight chain C_1-C_6 alkyl;

R_2 is selected from H, C_1-C_{10} alkyl, $C_4 - C_9$ cycloalkyl, $C_4 - C_9$ heterocycloalkyl, $C_4 - C_9$ heterocycloalkylalkyl, cycloalkylalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, $-(CH_2)_nC(O)R_6$, $-(CH_2)_nOC(O)R_6$, amino acyl, HON-C(O)-CH=C(R_1)-aryl-alkyl- and $(CH_2)_nR_7$;

R_3 and R_4 are the same or different and independently H, C_1-C_6 alkyl, acyl or acylamino, or R_3 and R_4 together with the carbon to which they are bound represent C=O, C=S, or C=NR_8, or R_2 together with the nitrogen to which it is bound and R_3 together with the carbon to which it is bound can form a $C_4 - C_9$ heterocycloalkyl, a heteroaryl, a polyheteroaryl, a non-aromatic polyheterocycle, or a mixed aryl and non-aryl polyheterocycle ring;

R_5 is selected from H, C_1-C_6 alkyl, $C_4 - C_9$ cycloalkyl, $C_4 - C_9$ heterocycloalkyl, acyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, aromatic polycycle, non-aromatic polycycle, mixed aryl and non-aryl polycycle, polyheteroaryl, non-aromatic polyheterocycle, and mixed aryl and non-aryl polyheterocycle;

n, n_1, n_2 and n_3 are the same or different and independently selected from $0 - 6$, when n_1 is 1-6, each carbon atom can be optionally and independently substituted with R_3 and/or R_4;

X and Y are the same or different and independently selected from H, halo, C_1-C_4 alkyl, NO_2, $C(O)R_1$, OR_9, SR_9, CN, and $NR_{10}R_{11}$;

R_6 is selected from H, C_1-C_6 alkyl, $C_4 - C_9$ cycloalkyl, $C_4 - C_9$ heterocycloalkyl, cycloalkylalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, OR_{12}, and $NR_{13}R_{14}$;

R_7 is selected from OR_{15}, SR_{15}, $S(O)R_{16}$, SO_2R_{17}, $NR_{13}R_{14}$, and $NR_{12}SO_2R_6$;

R_8 is selected from H, OR_{15}, $NR_{13}R_{14}$, C_1-C_6 alkyl, $C_4 - C_9$ cycloalkyl, $C_4 - C_9$ heterocycloalkyl, aryl, heteroaryl, arylalkyl, and heteroarylalkyl;

R_9 is selected from $C_1 - C_4$ alkyl and C(O)-alkyl;

R_{10} and R_{11} are the same or different and independently selected from H, C_1-C_4 alkyl, and -C(O)-alkyl;

R_{12} is selected from H, C_1-C_6 alkyl, $C_4 - C_9$ cycloalkyl, $C_4 - C_9$ heterocycloalkyl, $C_4 - C_9$ heterocycloalkylalkyl, aryl, mixed aryl and non-aryl polycycle, heteroaryl, arylalkyl, and heteroarylalkyl;

R_{13} and R_{14} are the same or different and independently selected from H, C_1-C_6 alkyl, $C_4 - C_9$ cycloalkyl, $C_4 - C_9$ heterocycloalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, amino acyl, or R_{13} and R_{14} together with the nitrogen to which they are bound are $C_4 - C_9$ heterocycloalkyl, heteroaryl, polyheteroaryl, non-aromatic polyheterocycle or mixed aryl and non-aryl polyheterocycle;

R_{15} is selected from H, C_1-C_6 alkyl, $C_4 - C_9$ cycloalkyl, $C_4 - C_9$ heterocycloalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl and $(CH_2)_mZR_{12}$;

R_{16} is selected from C_1-C_6 alkyl, $C_4 - C_9$ cycloalkyl, $C_4 - C_9$ heterocycloalkyl, aryl, heteroaryl, polyheteroaryl, arylalkyl, heteroarylalkyl and $(CH_2)_mZR_{12}$;

R_{17} is selected from C_1-C_6 alkyl, $C_4 - C_9$ cycloalkyl, $C_4 - C_9$ heterocycloalkyl, aryl, aromatic polycycle, heteroaryl, arylalkyl, heteroarylalkyl, polyheteroaryl and $NR_{13}R_{14}$;

m is an integer selected from 0 to 6; and

Z is selected from O, NR_{13}, S and S(O);

or a pharmaceutically acceptable salt thereof.

11. A combination for use in the treatment, prevention or suppression of an immune disorder, immune response or immune mediated response, or for the prevention or treatment of acute or chronic transplant rejection in a recipient patient of an organ, tissue or cell transplant, which comprises (a) a histone deacetylase inhibitor and (b) a second pharmacologically active agent in which (a) and (b) are present in each case in free form or in the form of a pharmaceutically acceptable salt or a pharmaceutically acceptable prodrug thereof, for simultaneous, concurrent, separate or sequential use.

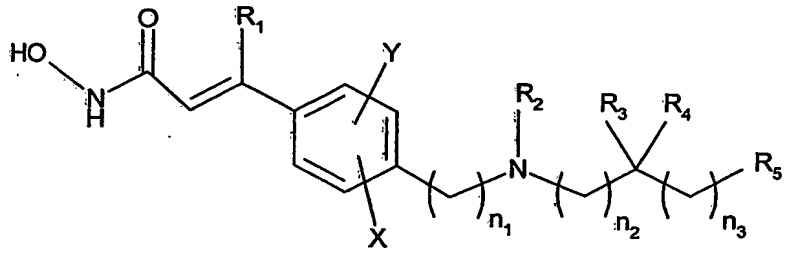
12. A combination of claim 11 wherein the second pharmacologically active agent is selected from the group according to claim 7 or 8.

13. The combination of claim 11 or 12 where the histone deacetylase inhibitor is a compound of formula (I) according to claim 10.

14. The combination of claim 13 wherein the histone deacetylase inhibitor is selected from the group consisting of N-hydroxy-3-[4-[[(2-hydroxyethyl)[2-(1H-indol-3-yl)ethyl]-amino]methyl]phenyl]-2E-2-propenamide, N-hydroxy-3-[4-[[[2-(1H-indol-3-yl)ethyl]-amino]methyl]phenyl]-2E-2-propenamide and *N*-hydroxy-3-[4-[[[2-(2-methyl-1*H*-indol-3-yl)-ethyl]-amino]methyl]phenyl]-2*E*-2-propenamide, or a pharmaceutically acceptable salt thereof or a pharmaceutically acceptable prodrug thereof.

15. A combination according to any one of claim 11-14 wherein the HDAI compound and the second pharmaceutically active agent are present synergistically effective amounts.

16. A method of treating, preventing or suppressing an immune disorder, immune response or immune mediated response of an animal comprising administering to said animal an effective amount of an histone deacetylase inhibitor compound of formula I:



(I)

wherein

R_1 is H, halo, or a straight chain C_1-C_6 alkyl;

R_2 is selected from H, C_1-C_{10} alkyl, $C_4 - C_9$ cycloalkyl, $C_4 - C_9$ heterocycloalkyl, $C_4 - C_9$ heterocycloalkylalkyl, cycloalkylalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, $-(CH_2)_nC(O)R_6$, $-(CH_2)_nOC(O)R_6$, amino acyl, HON-C(O)-CH=C(R_1)-aryl-alkyl- and $-(CH_2)_nR_7$;

R_3 and R_4 are the same or different and independently H, C_1-C_6 alkyl, acyl or acylamino, or R_3 and R_4 together with the carbon to which they are bound represent C=O, C=S, or C=NR_8, or R_2 together with the nitrogen to which it is bound and R_3 together with the carbon to which it is bound can form a $C_4 - C_9$ heterocycloalkyl, a heteroaryl, a polyheteroaryl, a non-aromatic polyheterocycle, or a mixed aryl and non-aryl polyheterocycle ring;

R_5 is selected from H, C_1-C_6 alkyl, $C_4 - C_9$ cycloalkyl, $C_4 - C_9$ heterocycloalkyl, acyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, aromatic polycycle, non-aromatic polycycle, mixed aryl and non-aryl polycycle, polyheteroaryl, non-aromatic polyheterocycle, and mixed aryl and non-aryl polyheterocycle;

n, n_1, n_2 and n_3 are the same or different and independently selected from 0 – 6, when n_1 is 1-6, each carbon atom can be optionally and independently substituted with R_3 and/or R_4;

X and Y are the same or different and independently selected from H, halo, C_1-C_4 alkyl, NO_2, $C(O)R_1$, OR_9, SR_9, CN, and $NR_{10}R_{11}$;

R_6 is selected from H, C_1-C_6 alkyl, C_4 – C_9 cycloalkyl, C_4 – C_9 heterocycloalkyl, cycloalkylalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, OR_{12}, and $NR_{13}R_{14}$;

R_7 is selected from OR_{15}, SR_{15}, $S(O)R_{16}$, SO_2R_{17}, $NR_{13}R_{14}$, and $NR_{12}SO_2R_6$;

R_8 is selected from H, OR_{15}, $NR_{13}R_{14}$, C_1-C_6 alkyl, C_4 – C_9 cycloalkyl, C_4 – C_9 heterocycloalkyl, aryl, heteroaryl, arylalkyl, and heteroarylalkyl;

R_9 is selected from C_1 – C_4 alkyl and C(O)-alkyl;

R_{10} and R_{11} are the same or different and independently selected from H, C_1-C_4 alkyl, and -C(O)-alkyl;

R_{12} is selected from H, C_1-C_6 alkyl, C_4 – C_9 cycloalkyl, C_4 – C_9 heterocycloalkyl, C_4 – C_9 heterocycloalkylalkyl, aryl, mixed aryl and non-aryl polycycle, heteroaryl, arylalkyl, and heteroarylalkyl;

R_{13} and R_{14} are the same or different and independently selected from H, C_1-C_6 alkyl, C_4 – C_9 cycloalkyl, C_4 – C_9 heterocycloalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, amino acyl, or R_{13} and R_{14} together with the nitrogen to which they are bound are C_4 – C_9 heterocycloalkyl, heteroaryl, polyheteroaryl, non-aromatic polyheterocycle or mixed aryl and non-aryl polyheterocycle;

R_{15} is selected from H, C_1-C_6 alkyl, C_4 – C_9 cycloalkyl, C_4 – C_9 heterocycloalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl and $(CH_2)_mZR_{12}$;

R_{16} is selected from C_1-C_6 alkyl, C_4 – C_9 cycloalkyl, C_4 – C_9 heterocycloalkyl, aryl, heteroaryl, polyheteroaryl, arylalkyl, heteroarylalkyl and $(CH_2)_mZR_{12}$;

R_{17} is selected from C_1-C_6 alkyl, C_4 – C_9 cycloalkyl, C_4 – C_9 heterocycloalkyl, aryl, aromatic polycycle, heteroaryl, arylalkyl, heteroarylalkyl, polyheteroaryl and $NR_{13}R_{14}$;

m is an integer selected from 0 to 6; and

Z is selected from O, NR_{13}, S and S(O);

or a pharmaceutically acceptable salt thereof.

17. A method for preventing or treating acute or chronic transplant rejection in a recipient patient of organ or tissue or cell transplant comprising the step of administering to said patient a therapeutically effective amount of a compound of formula (I) according to claim 16.

18. A method according to claim 16 or 17 further comprising a second pharmacologically active agent.

19. A method according to claim 18 wherein the second pharmacologically active agent is selected from immunosuppressive agents, immunomodulating agents, antibiotics, antiviral agents, steroids, NSAIDS or mixtures thereof.

20. A method for enhancing graft survival following transplant, comprising administering to an animal previous to, concurrently with, or subsequent to a transplant procedure an effective amount of an histone deacetylase inhibitor compound of formula I according to claim 15.